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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,180	07/30/2003	Zheng Wei	10709/47	9214

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02/20/2007

EXAMINER
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DEBERRY, REGINA M

ART UNIT	PAPER NUMBER
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1647

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/20/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

## Office Action Summary

Application No.

10/630,180

Applicant(s)

WEI, ZHENG

Examiner

Regina M. DeBerry

Art Unit

1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 22 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-62 is/are pending in the application.
- 4a) Of the above claim(s) 55-60 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-54, 61 and 62 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date See Continuation Sheet.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :10/03,6/04,3/05,5/05,11/05,6/06,11/06.

***Status of Application, Amendments and/or Claims***

The amendment filed 22 November 2000 has been entered in full. New claims 61 and 62 were added.

Applicant's election of Group I (claims 1-54) in the reply filed on 22 November 2006 is acknowledged. Applicant argues that Group II is stated by the Office Action to be directed to an apparatus, which apparatus can be alternatively used for assessment of tumor invasiveness, without providing any support in technical or patent literature. Applicant states that Group II is directed to a kit that includes an apparatus *inter alia*, and not to an apparatus per se. Applicant states that the kit described in the claims of Group II has only the one use as far as applicants know, to perform the claimed method. Applicant states, "as such claim 55 was amended to clarify that the kit is for detecting chemokine receptor antagonist". Applicant argues that appropriate reasoning for dividing among related inventions has not been provided. Applicant cites MPEP 808.02.

Applicant has not explicitly stated for the record that Group I was elected with traverse. Nevertheless, because Applicant has pointed out the supposed errors in the restriction requirement, the Examiner assumes that Applicant has elected Group I (claims 1-54) with traverse.

Applicant's arguments have been fully considered but are not found persuasive. MPEP 808.02, as cited by Applicant, states when the inventions as claimed are shown to be independent or distinct under the criteria of MPEP 806.05(c)-806.06, the

Examiner, in order to establish reasons for insisting upon restriction, must show by appropriate explanation **one of the followings**: Separate classification thereof, separate status in the art when they are classifiable together or a different field of search. Group II (claims 55-60) has a separate status in the art and a different field of search from Group I. Group II is directed to a kit comprising an apparatus AND various chemokines. A search for a chemokine and an apparatus is not co-extensive with a search for a method of identifying chemoattractant receptor antagonists. A search for the two Groups would not employ the same search or techniques to identify documents relevant to patentability. A kit comprising chemokines and an apparatus is a different technology and would not completely overlap with the technology for a method for identifying chemoattractant receptor antagonists. Furthermore, the intended use or process limitations added to the kit claims are given no patentable weight with respect to the kit product except as they define the components of the kit. As such, it would be burdensome to search the inventions of Groups I and II together.

The requirement is still deemed proper and is therefore made FINAL. Claims 55-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 22 November 2006. Claims 1-54, 61 and 62 are under examination.

***Information Disclosure Statement***

The information disclosure statement(s)(IDS) filed 10/30/03, 6/09/04, 3/21/05, 5/12/05, 11/21/05, 6/05/06 and 11/22/06 were received and comply with the provisions of 37 CFR §§1.97 and 1.98. They have been placed in the application file and the information referred to therein has been considered as to the merits.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-54, 61 and 62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant invention is drawn to the reverse activation of migration (RAM) assay. The specification teaches that the RAM assay identifies and discriminates antagonists while decreasing the prevalence of false positives and negatives signals found in other assays. The specification teaches that conventional screens for antagonists of cell migration measure the reduction of cell migration; the RAM assay measures the activation of cell migration. In the RAM assay, cells are challenged to migrate in the presence of migration-inhibitory concentrations of chemoattractants in response to

candidate antagonists. The purported novelty of the instant invention is that the RAM assay identifies and discriminates antagonists while decreasing the prevalence of false positives and negatives signals found in other assays using set parameters. Ligands induce cell migration, but at inhibitory concentration certain ligand inhibits cell migration. The specification teaches that when a cell migrates in the presence of a candidate antagonist and an inhibitory concentration of the ligand, the candidate antagonist is identified as a true antagonist. For example the examples teach chemokine stromal-derived factor (SDF-1) as a ligand for chemokine receptor CXCR4. SDF-1 induces cell migration, but at higher concentrations of SDF-1, cell migration is inhibited. The specification identifies vMIP-II as an antagonist by using a conventional cell migration assay where cell migration was induced by SDF ligand but inhibited with increasing amounts of vMIP-II (Examples 1-2). In the RAM assay, cells are challenged to migrate in the presence of migration-inhibitory concentrations of chemoattractants in response to true antagonists.

The specification teaches that in a binary RAM (BiRAM) assay, two types of chemoattractant receptors can be assayed in the same assay. Either a single cell population comprising two different receptors on one cell or two distinct cell populations each comprising a different receptor are incubated with a candidate antagonist and then contacted with an inhibitory concentration of ligands for the target receptor. The ability of the cell populations to migrate in response to the treatment with a candidate antagonist is assayed. If the cell migrates in the presence of a candidate antagonist, then a positive signal is observed (page 12, lines 1-10; page 18, lines 5-21 and page

19, line 1-page 20, line 30). In a MultiRAM screening assay, multiple types of chemoattractant receptors can be assayed in the same assay. Either a single cell population comprising multiple different chemokine receptors or multiple cell populations comprising different receptors each are incubated with a candidate antagonist and then contacted with an inhibitory concentration of ligands for the target receptor. The ability of the cell populations to migrate is then assayed. If the cell migrates in the presence of a candidate antagonist then a positive signal is observed (page 12, lines 1-10 and page 21, line 10-page 22, line 5).

The instant claims are drawn to BiRAM and MultiRAM assays. Example 8 teaches the BiRAM assay. THP-1 cells express cell surface CCR1 and CCR2 receptors. MIP-1alpha and MCP-1 are ligands for CCR1 and CCR2 respectively (page 37, lines 6-15). The specification teaches that BiRAMAG1 and BiRAMAG2 are used as CCR1 and CCR2 antagonists, respectively. THP-1 cell migration in response to BiRAMAG1 was observed. THP-1 cell migration in response to BiRAMAG2 was observed (Figure 12A-B). The specification states that these results provide support for the BiRAM assay using cell population expressing two chemokine receptors being capable of detecting antagonists of these chemokine receptors.

The instant claims are not enabled because the specification fails to teach how to identify **unknown candidate antagonists** and the chemoattractant receptors causing the cell migration. The BiRAM and MultiRAM assays employ more than one chemoattractant receptor and at least two candidate antagonists (claims 2, 29). For example, if more than one candidate antagonist (**i.e. it is truly unknown if the agents**



are antagonists) is placed with the cell population in the upper chamber, how does one skilled in the art discern *which candidate antagonist* is inducing the cell population migration to the lower chamber? Furthermore, if a single cell population comprising multiple different chemokine receptors or multiple cell populations comprising different receptors each are incubated with a candidate antagonist (or candidate antagonists) in the upper chamber, how does one skilled in the art discern *which chemoattractant receptor(s)* is inducing the cell population migration to the lower chamber. The instant examples employ known antagonists to known chemoattractant receptors. The instant examples do not teach the incubation of *an unknown candidate antagonist(s)* together with a cell population comprising more than one chemoattractant receptor in the upper chamber, wherein incubation induces cell population migration to the lower chamber in the presence of inhibitory concentrations of ligands of the chemoattractant receptors wherein the unknown candidate antagonist(s) is identified as a true antagonist and its chemoattractant receptor(s) is identified. The specification fails to teach how the said antagonist(s) and its chemoattractant receptor(s) is identified. The teachings in the examples are not tantamount to the instant claims.

Due to the large quantity of experimentation necessary to identify a candidate antagonist(s) as a true antagonist and its chemoattractant receptor(s), the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite limitations regarding parameters for identifying unknown candidate antagonists and its chemoattractant receptors, undue

experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite because of the interchangeable use of "**placing** a candidate antagonist and a cell population" (claims 1, 2, 19-21, 28, 29, 46-48, 54) and "**incubating** a candidate antagonist and a cell population" (claim 27). It is unclear from the specification, the difference between "placing" and "incubating". Applicant is asked to **specifically point in the specification**, the difference between "placing" and "incubating".

### ***Claim Objections***

Claims 27, 28 and 54 are objected to because of the instant claims comprise very similar steps:

a method wherein two cell populations (each with a chemoattractant receptor) are incubated with a candidate receptor in the upper chamber, inhibitory concentrations

of a ligand for the first cell population and the second population are placed in the lower chamber migration of the first and second cell population from the upper chamber to the lower chamber is assayed, wherein movement identifies the candidate antagonist as an antagonist of either the chemoattractant for the first cell population or a chemoattractant receptor for the second population or both.

The instant claims raise the question of similar scope. The Examiner has examined the specification and cannot figure out the difference between the claims. If the claims are not of similar scope, Applicant is asked to **specifically point in the specification**, the patentable distinction between the claims.

### ***Conclusion***

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
RMD  
1/7/07

  
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